repeat-recognising telomere capping complex, called shelterin. Instead a new complex, named terminin has evolved in *Drosophila melanogaster* and closely related species, which has an essential role in telomere capping and maintenance. Genes encoding proteins involved in this complex, appeared recently in the phylogenesis and since then these genes have been quickly changing. The proteins are functional analogues of the members of shelterin complex. Terminin complex (just like shelterin) interacts with proteins involved in the DNA damage signaling pathways. The lack of either capping proteins causes telomere disruption, therefore activates DNA damage checkpoints and fuses the end of the chromosomes.

The bicistronic *Drosophila* gene *dtl/tgs1* (*CG31241*) encodes two proteins; *Drosophila Tat-Like/Drosophila Telomere Lost* (DTL) – is a member of the telomer protecting terminin complex, and *Trimethyl-Guanin Synthase* (TGS1) that catalyzes the trimethyl-guanine (TMG) cap synthesis of sn- and snoRNAs (Komonyi et al 2005. and 2009). Our data indicate, that both products of *dtl/tgs1* gene are essential. Mutations which affected *dtl* (but didn't have any effect on *tgs1)* caused telomere associations (TAs), whereas the absence of TGS1 (but not DTL), resulted defected TMG cap containing RNA synthesis. However, DTL and TGS1 seem to have distinct functions such as telomere maintenance and RNA processing, these two functions might possibly be interconnected as TMG cap containing RNAs play an important role in telomere maintenance.

We payed particular attention to determine the role of the two proteins in the germ line. In the lack of maternal *dtl/tgs1* product, the development of eggs is significantly abnormal. After fertilisation, erratic cleavage division can be observed and only a few embryos reach the zygotic expression stage. For better understanding, we have investigated the unique effect of either the DTL or the TGS1 protein during oogenesis.

Since DTL is a putative member of terminin complex, we have supposed that it interacts with proteins involved in telomere maintenance. Therefore, we have performed yeast two hybrid experiments to find possible interacting partners. We have overexpressed FLAG epitop-labelled DTL in transgenic flyes in order to purify DTL containing complex and other interacting partners.

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The role of Rac1 in stress signaling

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The heat shock response (HSR), one of the most studied cellular homeostatic mechanisms, is involved in the maintenance of cell functionality during stress. Yet, the whole stress signaling pathway has not been elucidated. In line with the membrane thermosensor model, mild stress, or "membrane defects" caused by different disease states, is sensed by changes in the fluidity and microdomain structure of membranes, influencing membrane localized signaling activities. In favor of this model, our group exposed different mammalian cells to various membrane fluidizers or drugs with the ability to interact with certain membrane lipids and found substantial modulation of heat shock protein (Hsp) expression. One possible signaling pathway originating from plasma membrane involves the lipid kinase, PI3kinase, which in turn activates the small GTPase, Rac1. Through downstream signaling cascade to MAP kinases, the main transcription factor, HSF1 is activated leading to Hsp synthesis. It was shown that Rac1 translocation to the plasma membrane is essential for activating downstream effectors and its membrane binding is determined at least in part by membrane lipids. In favor of "membrane stress sensor" model, our working hypothesis was that Rac1 pathway is involved in stress signaling through the effect of stress on membrane microdomain organization.

To study Rac1 involvement in HSR, we created tetracycline inducible stable mutant B16-F10 cells which are either dominant negative or constitutively active for Rac1. Though the antibiotic resistance showed stable clones, Rac1 protein expression was not detectable after induction. Now we use the "Sleeping Beauty Transposon" for stable Rac1 gene transfer in B16F-10cells.

As a proof of concept we have shown that using specific Rac1 inhibitor, NSC23766 and Capsaicin, the heat shock response decreased remarkably in dose dependent manner. Moreover, elevated levels of heat shock response achieved by addition of a Hsp co-inducer, BGP-15 is diminished by Rac1 inhibitors. We also documented that the amount of phosphorylated, active transcription factor, HSF1 decreased in inhibitor treated samples. In order to document the different localization of Rac1 in heat treated B16 cells we made immunofluorescence microscopy and Western blots on isolated membrane fractions.

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